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Gegen Qinlian Decoction in experimental murine ulcerative colitis: a preclinical systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - This research was supported by the institutional resources of the Department of Histology, Faculty of Medicine, Autonomous University of Nuevo León.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 September 2025 and was last updated on 20 September 2025.

INTRODUCTION

Review question / Objective The primary objective of this systematic review and meta-analysis is to determine the efficacy of aqueous Gegen Qinlian Decoction (GQD) in murine models of dextran sodium sulfate (DSS)-induced ulcerative colitis.
Using the PICO framework:
Population: Mice with DSS-induced ulcerative colitis.
Intervention: Gegen Qinlian Decoction (GQD), administered as either an aqueous or ethanolic extract.
Comparator: DSS-only control group (placebo or no treatment).
Outcomes: The primary outcome is the Disease Activity Index (DAI). Secondary outcomes include colon length and histological score.
Secondary objectives include exploring sources of heterogeneity through pre-specified subgroup analyses based on dose (<7.5 g/kg vs. ≥7.5 g/kg) and extract type (aqueous vs. ethanolic). Additionally, an exploratory meta-regression will be conducted to investigate the dose-response relationship for the primary outcome. The robustness of the primary outcome's pooled estimate will be assessed using a leave-one-out sensitivity analysis.

Rationale Ulcerative colitis (UC) is a chronic inflammatory bowel disease with a rising global prevalence and a significant impact on patients' quality of life. While current pharmacological treatments have advanced, they are associated with limitations including incomplete efficacy, adverse effects, and high costs, highlighting a persistent need for safer and more accessible therapeutic alternatives.
Gegen Qinlian Decoction (GQD), a traditional Chinese medicine formula, has shown biological plausibility for treating UC, with preclinical reports

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suggesting anti-inflammatory and gut barrier-protective mechanisms. However, existing clinical meta-analyses evaluating GQD have been assessed as having "critically low" methodological quality, which prevents firm conclusions for clinical practice.
Therefore, a rigorous preclinical systematic review is warranted to synthesize the foundational evidence for GQD's efficacy in standardized animal models. This will help to clarify the consistency of its effects and inform the design of future, higher-quality clinical trials.

Condition being studied Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease (IBD) characterized by diffuse mucosal inflammation limited to the colon and rectum. The inflammation typically begins in the rectum and can extend proximally in a continuous manner. Clinical manifestations primarily include persistent bloody diarrhea, abdominal pain, and fecal urgency. The disease course is marked by periods of active disease and remission. Long-standing and extensive UC significantly impairs health-related quality of life and is associated with an increased risk of developing colorectal cancer.

METHODS

Search strategy A systematic search was conducted in PubMed, Scopus, and Web of Science up to July 2025. The search strategy combined keywords and controlled vocabulary (e.g., MeSH) related to the intervention ('Gegen Qinlian Decoction'), the condition ('ulcerative colitis', 'inflammatory bowel disease'), and the model ('dextran sulfate sodium', 'DSS', 'mouse', 'murine'). The reference lists of included studies and relevant reviews were also manually screened for additional records.

Participant or population The population of interest consists of mice of any strain, sex, or age in which an experimental model of ulcerative colitis has been induced using Dextran Sodium Sulfate (DSS).

Intervention The primary intervention of interest is the traditional aqueous decoction of GQD. Studies using ethanolic extracts will also be included for a separate, exploratory subgroup analysis. Only studies utilizing oral gavage as the route of administration will be considered. Any dose and duration of treatment will be included.

Comparator The comparator group consists of mice with DSS-induced colitis that do not receive the active GQD intervention. This includes control groups that receive a placebo (e.g., saline, distilled water, or vehicle) or no treatment, while still being subjected to the same DSS colitis induction protocol as the intervention group.

Study designs to be included Only preclinical, in vivo, controlled experimental animal studies will be included.

Eligibility criteria In addition to the PICO criteria, studies must be published in a peer-reviewed journal. Only articles written in the English language will be included. Review articles, studies lacking a DSS-only control group, and studies from which quantitative data (mean and standard deviation) cannot be reliably extracted will be excluded.

Information sources The primary information sources will be the electronic databases of PubMed, Scopus, and Web of Science. Additionally, the reference lists of all included studies and relevant review articles will be manually screened to identify any potential additional studies. In cases of missing or unclear data, we will attempt to contact the corresponding authors of the primary studies via email for clarification.

Main outcome(s) The primary outcome is the Disease Activity Index (DAI). This is a composite clinical score used to assess the severity of colitis, calculated from scores for weight loss, stool consistency, and rectal bleeding. The effect measure will be the Standardized Mean Difference (SMD) with 95% Confidence Intervals (CI), analyzed at the end of the study period.

Additional outcome(s)
The pre-specified secondary outcomes are:
1. Colon Length: A macroscopic measurement of colonic inflammation and edema, measured in centimeters at sacrifice. The effect measure will be the Mean Difference (MD) with 95% CI.
2. Histological Score: A microscopic assessment of tissue damage, including inflammatory infiltrate and epithelial injury. The effect measure will be the Standardized Mean Difference (SMD) with 95% CI.

Data management Search results will be managed and screened in the Rayyan web application. Screening of titles, abstracts, and full texts will be performed independently by two reviewers.
A standardized form in Microsoft Excel will be used for data extraction, also in duplicate. In cases where numerical data for outcomes are presented only in graphical format and not reported in the

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text or tables, values will be extracted using WebPlotDigitizer. This graphical data extraction will also be performed independently by two reviewers. Discrepancies will be resolved by consensus or by a third author.

Quality assessment / Risk of bias analysis The risk of bias in included studies will be assessed independently by two reviewers using the SYRCLE (Systematic Review Centre for Laboratory animal Experimentation) tool. Each of the 10 domains will be judged as 'Low risk', 'High risk', or 'Unclear risk' of bias. Disagreements will be resolved through discussion. The results will be presented in a summary table and a risk-of-bias summary graph.

Strategy of data synthesis The primary data synthesis will focus on the cohort of studies that used aqueous GQD extracts. Studies using ethanolic extracts will be analyzed separately and in a comparative subgroup analysis to explore sources of heterogeneity. Meta-analyses will be performed using R software (metafor package) and primarily RevMan 5.4. For the primary outcome (DAI) and histological score, the effect measure will be the Standardized Mean Difference (SMD) with 95% Confidence Intervals (CI). For colon length, the Mean Difference (MD) with 95% CI will be used. A random-effects model, using the Restricted Maximum-Likelihood (REML) estimator, will be used to pool the data for all outcomes. Statistical heterogeneity will be assessed using the Cochrane's Q test (Chi^2) and quantified with the I^2 statistic. A p-value of < 0.05 will be considered statistically significant.

Subgroup analysis To investigate potential sources of heterogeneity, pre-specified subgroup analyses will be conducted for each outcome, stratifying by: (1) dose of GQD (low-dose < 7.5 g/kg vs. high-dose ≥ 7.5 g/kg); and (2) type of extract (aqueous vs. ethanolic). The analysis comparing extract types is intended to formally test for differences in effect size and consistency.
Additionally, for the primary outcome of the aqueous cohort, an exploratory random-effects meta-regression will be conducted to assess the linear relationship between treatment effect and dose as a continuous variable. The significance of differences between subgroups will be assessed using the test for subgroup differences.

Sensitivity analysis To assess the robustness of the findings for the primary outcome (DAI), a leave-one-out sensitivity analysis will be performed. This analysis involves iteratively removing one study at a time and recalculating the pooled effect estimate to determine if any single study has a disproportionate influence on the overall result.

Language restriction Yes, the review is limited to articles published in the English language.

Country(ies) involved México.

Other relevant information The protocol was initially registered on the Open Science Framework (OSF) (DOI: 10.17605/OSF.IO/A8H3W) prior to the formal data extraction and synthesis. This more comprehensive registration on INPLASY was completed while the final data analysis and interpretation were being conducted.

Keywords Gegen Qinlian Decoction; Ulcerative Colitis; Systematic Review; Meta-analysis; Preclinical; Murine Model; DSS.

Dissemination plans The findings of this systematic review and meta-analysis will be disseminated through publication in a peer-reviewed scientific journal and presentation at a relevant scientific conference.

Contributions of each author

Author 1 - Carlos Roberto Montes-de-Oca-Saucedo - Conceptualization; Methodology; Data Curation (literature search, screening, extraction, and risk of bias assessment); Formal Analysis (statistical analysis); Investigation; Visualization; Writing – Original Draft; Writing – Review & Editing.
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